REMARKS

Upon entry of this preliminary amendment, Claims 34-47 are the pending claims. These claims are directed to medical devices, including catheters and stents, comprising a nucleic acid encoding a wild-type human kinase interacting stathmin (hKIS) protein or a nucleic acid encoding an hKIS protein that contains a mutation reducing its serine/threonine kinase activity and that inhibits phosphorylation of p27, each protein comprising the specified sequence. Support for these claims is found in the Specification at pages 32-33. No new matter has been added.

I. Explanation Of Specification Amendments

Applicants are amending three obvious errors found in the specification in the paragraph at page 43, line 22 to page 44, line 3. First, SEQ ID NO. 1 represents a nucleic acid sequence, but as used in the context of the third sentence of this paragraph, it is confusing. Accordingly, the sentence is reworded to clarify that the percent identity refers to amino acid sequences and not to nucleic acid sequences so the sentence now provides that the "clone (SEQ ID NO. 1), C21, encodes a polypeptide that was 99% similar to the rat serine/threonine protein kinase . . . ." As rewritten, the sentence is a statement of fact and no new matter has been introduced. Second, the word "was" was omitted from the phrase "it was concluded" (at line 6) which is a clear typographical error. Third, the cited reference for the rat sequence was inadvertently indicated as Zamore (Zamore *et al.*, 1992, Nature 355:609) when it is actually the Maucuer reference and GenBank accession number (of record). The Zamore reference relates to hU2AF65, a 65kDa subunit of the splicing factor U2AF, a protein distinctly different from rat KIS, as that reference makes clear (abstract enclosed) and as stated in the same paragraph (four lines below the

erroneous cite). Similarly, the Maucuer reference clearly discloses the rat KIS sequence. Accordingly, correction of these errors are believed to be proper and do not introduce new matter.

II. Explanation of Replacement Sequence Listing

This substitute Sequence Listing is submitted to correct errors in the hKIS protein sequences designated as SEQ ID. NOS. 2 and 4. No changes have been made in the other sequences. This error was discovered during review of the Sequence Listing in preparation for filing this divisional application. The corrected sequences are fully supported by the co-pending, parent application as originally filed (U.S. Serial No. 09/378,517, filed August 20, 1999) and, as explained below, do not present new matter.

In particular, new SEQ ID. NOS. 2 and 4 differ from those presented in the parent Sequence Listing by the addition of one amino acid. For both sequences, amino acid 187 is added and is glutamine (represented in three-letter code as "Gln" or in one-letter code as "Q"). The length of the protein sequences in both instances is now 419 amino acids.

A. SEQ ID NO. 2

In the present and originally-filed parent Sequence Listing submissions,[1] the nucleic acid sequence for wild-type hKIS is provided in SEQ ID NO. 1. Translation of this nucleotide sequence encodes a protein of 419 amino acids in length.[2] However, SEQ ID NO. 2 of the original submission was only 418 amino acids long. A comparison of the amino acid sequence from SEQ ID NO. 2 with the translated amino acid sequence from SEQ ID NO. 1 showed that the only difference was the change noted and corrected above, *i.e.*, that glutamine 187 encoded

[1] Applicants submitted a request to correct the Sequence Listing in the parent application.
[2] SEQ ID NO. 1 is 1260 nucleotides long, which represents 420 codons. The sequence starts with ATG (encoding methionine) and ends with TAA (a stop codon). Accordingly, the encoded hKIS protein from this nucleotide sequence is 419 amino acids in length.

in SEQ ID NO. 1 was not included in SEQ ID NO. 2. Accordingly, it appears that one amino acid was inadvertently dropped (omitted) during preparation of the original Sequence Listing in the parent application.

This sequence difference appears to have arisen as an inadvertent error and does not represent new matter as those of skill in the art would understand that amino acid 187 is present (and is glutamine) based on an analysis of the nucleotide sequence provided by SEQ ID NO. 1. Furthermore, that Gln 187 is part of the amino acid sequence of hKIS is supported by the provisional application (U.S. Serial No. 60/097,710, filed August 21, 1998) to which both the parent and the present application properly claim priority and which are both incorporated by reference into the present application.

In particular, the provisional application expressly states that hKIS is a protein of 419 amino acids:

> The DNA segments and vectors may comprise an isolated gene or coding sequence that encodes a hKIS protein characterized as having the following properties:
>
> Being about 419 amino acids in length;
>
> Comprising an amino-terminal kinase domain, preferably a kinase domain that phosphorylates p27;
>
> Comprising a carboxy-terminal RNA binding domain; and
>
> Binding to p27, as may be assessed by one or more cellular assay systems, . . .

(Page 2, Line 29 to Page 3, Line 5);

> Wild type, polymorphic or mutant hKIS proteins may be full length proteins, such as being 419 amino acids in length.

(Page 57, Lines 3-4); and further provides both a nucleic acid and an amino acid sequence for wild-type hKIS in Examples 2 and 3, respectively, wherein both sequences provide that hKIS is

419 amino acids long (Page 87).[3] The nucleotide sequence in the provisional application is identical to that in the parent and present applications and thus also provides that amino acid 187 is glutamine.

The protein sequence in the provisional application is identical to that in the parent and present applications but for amino acid 187. In the provisional application, the hKIS amino acid sequence is provided in one-letter amino acid symbols with amino acid 187 indicated as "O" – which is not a one-letter symbol used for any of the 20 standard L-amino acids incorporated into protein (via translation of mRNA). The use of "O" is readily apparent as a typographical error to those of skill in the art (it should have been "Q") and may explain why the later-prepared Sequence Listing came up one amino acid short. Moreover, Patent-In 2.0, the program used to prepare the original Sequence Listing in the parent application, ignores and fails to recognize any non-standard one-letter amino acid symbols and would have dropped the "O" out of the sequence resulting in SEQ ID NO. 2 being one amino acid shorter. No matter the cause for the sequence error, Applicants believe that it would be unambiguous to those of skill in the art from both the present specification, the parent application and the provisional application that (1) wild-type hKIS is a protein of 419 amino acids and (2) that the nucleotide sequences in each application establish that amino acid 187 of hKIS is glutamine. Accordingly, no new matter is presented and correction of SEQ ID NO. 2 is respectfully requested.

B. SEQ ID NO. 4

SEQ ID NO. 2 presents the amino acid sequence for wild-type hKIS whereas SEQ ID NO. 4 presents the amino acid sequence of a mutant hKIS. These proteins differ from each other at a single amino acid residue, namely lysine 54 of the wild-type sequence is replaced by

[3] For convenience of the Examiner, Applicants enclose copies of the relevant pages of the provisional application. Applicants are happy to provide a complete copy of the provisional application upon request but have not done so to avoid unnecessarily burdening the filewrapper since the Examiner can obtain and examine that the provisional application at the PTO if deemed necessary. The enclosures herewith include the PTO sheet with filing particulars, the PTO Fee Record Sheet, Applicants' Provisional Application Cover Sheet, and Provisional Application Pages 1-3, 57 and 87.

arginine (K54R mutant). This specific mutant hKIS was not disclosed in the provisional application but is disclosed in the parent application.

Nonetheless and as above for the wild-type hKIS, the nucleic acid sequence (SEQ ID NO. 3) for the K54R mutant encodes a protein of 419 amino acids with amino acid 187 being glutamine as shown by translation of that nucleic acid sequence. Similar to the situation with wild type hKIS, the amino acid sequence (SEQ ID NO. 4) for the K54R mutant is 418 amino acid long and lacks the same amino acid (Gln 187) in the original Sequence Listing submission of the parent application. Except for the change to create the mutant at residue 54, the wild-type and K54R amino acid sequences are identical. Hence, Applicants believe that those of skill in the art would clearly and unambiguously appreciate that amino acid 187 of the K54R mutant is glutamine. Accordingly, appropriate correction of SEQ ID NO. 4 (to add amino acid 187 as glutamine) does not present new matter and is respectfully requested.

CONCLUSION

Early entry of this amendment and favorable consideration are respectfully requested. The Examiner is invited to contact the undersigned by telephone should any questions arise.

Respectfully submitted,

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